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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/657,431 | 09/07/2000 | Dominique P. Bridon | REDC-2201 USA | 1545 |
| 20872 | 7590 | 12/17/2003 | EXAMINER | |
| MORRISON & FOERSTER LLP 425 MARKET STREET SAN FRANCISCO, CA 94105-2482 | | | CHISM, BILLY D | |
| | | ART UNIT | PAPER NUMBER | |
| | | 1654 | | |

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|---------------------------|------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/657,431 | BRIDON ET AL. |
| | Examiner B. Dell Chism | Art Unit 1654 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 17 September 2003.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-16 and 19-21 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-16 and 19-21 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) The translation of the foreign language provisional application has been received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.

4) Interview Summary (PTO-413) Paper No(s) _____.

5) Notice of Informal Patent Application (PTO-152)

6) Other: _____.

DETAILED ACTION

This office action is in response to Applicants' response filed 17 September 2003.

Withdrawal of Objections and Rejections

The rejections and/or objections made in the prior office action, which are not explicitly stated below, in original or modified form are withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Applicants' arguments filed 17 September 2003 will be addressed to the extent that they pertain to the present grounds of rejection.

Claim Rejections - 35 USC § 112

1. Claims 7-16 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are rejected for the indefinite recitation of the term "derivative" wherein it is unclear what a derivative is. The specification does not differentiate between a derivative and a modified kringle 5, especially wherein it appears that there are two different compounds, one being a 'modified kringle 5' and the other being a 'derivative of the modified kringle 5'. It is suggested that the Applicants maintain the language of "modified" and delete references to "derivatives".

2. Claims 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. The claims lack antecedent basis for the recitation of the term “peptide” when referencing parent claim 10. Claims 11-12 are drawn to the derivative of a kringle 5 peptide.

3. Claims 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims lack antecedent basis for the recitation of the term “peptide” when referencing parent claim 13. Claims 14-17 are drawn to the derivative of an antiangiogenic peptide.

4. Claims 7-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the composition comprising a modified kringle 5 peptide, does not reasonably provide enablement for the intended use whereby the composition is used for in vivo treatment of angiogenesis in humans. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, “The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...”. The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring “ingenuity beyond that to be expected of one of ordinary skill in the art” (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150

(CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (*In re Marzocchi*, 169 USPQ 367 (CCPA 1971)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Colianni*, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986), and are summarized in *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988)). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to a composition comprising a [derivative] of a kringle 5 peptide for the intended in vivo usage for humans.

The state of the prior art and the predictability or lack thereof in the art: Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The art teaches that data from in vitro use of cancer therapeutics on cell lines do not capitulate adequately into clinical in vivo studies for humans (Dermer, G.B. 1994, Bio/Technology Vol. 12, page 320). Therefore, there is a lack of predictability regarding the intended use of the instantly claimed composition for in vivo treatment of humans in need of treating angiogenesis.

The amount of direction or guidance present and the presence or absence of working examples: Given the teachings found in the art regarding the deficiencies of cell culture data capitulating to clinical and therapeutic in vivo uses of cancer therapeutics for humans, detailed guidance is required in the specification to enable one of skill in the art to be able to use the claimed compositions. This guidance is absent. The specification contains only cell line culture assays (pages 65-66). There is no guidance as to how to administer any of the [derivatives] of a kringle 5 peptides for treatment of angiogenesis or what effects are to be expected or what patient population is to receive the composition being administered. There are no working examples directed to in vivo treatment of angiogenesis in humans in need thereof.

The breadth of the claims and the quantity of experimentation needed: Given the teachings of unpredictability which are found in the art regarding the therapeutic efficacy of any compositions having been tested only in vitro on cell cultures being used for in vivo treatments for cancer in humans, and in the absence of sufficient guidance in applicant's disclosure to overcome the teachings of unpredictability which are found in the art, it would require undue experimentation by one of skill in the art to be able to use the claimed invention.

5. (New) Claims 7-16 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "written description" rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination

of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the "written description" inquiry, is *whatever is now claimed*" (see page 1117).

A review of the language of the claim indicates that these claims are drawn to a genus, i.e., the genus of derivatives of a kringle 5. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention".

There are insufficient species of the claimed genus disclosed that are within the scope of the claimed genus, which is drawn to any/all possible modified angiogenic peptides. The

disclosure of one or two species may provide an adequate written description of a genus when the species disclosed are representative of the genus. However, the present claim encompasses numerous species that are not further described.

One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus of derivatives of modified kringle 5 peptides or derivatives of non-modified kringle 5 peptides. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (see *Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

6. Claims 1-16 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "written description" rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the "written description" inquiry, is *whatever is now claimed*" (see page 1117).

A review of the language of the claim indicates that these claims are drawn to a genus, i.e., the genus of modified antiangiogenic peptides and compositions comprised thereof. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention".

There are insufficient species of the claimed genus disclosed that are within the scope of the claimed genus. The disclosure of one or two species may provide an adequate written description of a genus when the species disclosed are representative of the genus. However, the present claim encompasses numerous species that are not further described. The specification only discloses modified **kringle 5 peptides** with claimed antiangiogenic activity, and does not disclose any other modified antiangiogenic peptides and compositions thereof. The specification

Art Unit: 1654

discloses structures and amino acid formulas for **modified kringle 5 peptides** only, and does not disclose any other modified antiangiogenic proteins, i.e., hemostatic proteins.

One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus of all possible modified antiangiogenic peptides. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (see *Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Conclusions

No claims are allowed. The subject matter indicated to be allowable in the previous office action, mailed 17 June 2003, is now rejected as described above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to B. Dell Chism whose telephone number is 703-306-5815. The examiner can normally be reached on 7:30 AM - 4:30 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 703-306-3220. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

B. Dell Chism
15 December 2003

Brenda Brumback
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